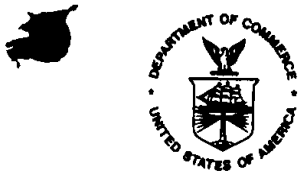

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/360,242	07/22/99	MCDONALD	J 25020-601B

VB

HM12/0302

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1646	10

DATE MAILED: 03/02/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/360,242	Applicant(s) MCDONALD ET AL.	
	Examiner Robert Landsman	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *17 December 1999* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-40 and 42-64* is/are pending in the application.

4a) Of the above claim(s) *39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-38,40 and 43-64* is/are rejected.

7)☒ Claim(s) *25,29-34,37,38,41,42,46,50,53,54,60,63 and 64* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☒ Notice of References Cited (PTO-892)
15) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
17) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☐ Other:

DETAILED ACTION

A. The IDS, filed 11/12/99, has been entered into the record.

B. The supplemental Information Disclosure Statement was received 12/7/99 and entered into the record.

C. Amendment B, filed 12/17/99, has been entered into the record.

D. A corrected computer disk containing the CRF was received 12/17/99 and entered into the record.

E. Claims 1-41 were pending in the instant application and were subject to restriction. Applicants elected Group II, claims 25-39. Applicants further request that Group III, claim 40, be examined with Group II. The Examiner agrees to examine Groups II and III, and, therefore, claims 25-40. Applicants have since added claims 42-64. Claim 39 is withdrawn since the targeted agent is a nucleic acid, and Applicants have elected a toxin as their species of targeted agent. The Examiner has agreed to examine claims 25-38, 40 and 42-64 in the present application.

1. Specification

F. The specification is objected to since:

On page 29, line 21, the term "protesins" is misspelled.

On Page 37, line 15, the excess spacing between the sentences should be removed.

The Brief Description of Drawings for Figure 1 is not referenced as "Figure 1A," "Figure 1B" and "Figure 1C" to correspond to the Figure.

The titles at the top of Figures 2-5 do not correspond to the vector names of each drawing in the Figure, or in the Brief Description of Drawings. For example, Figure 2 is referenced as "pGEMEX-SAP" in the title and in the Brief Description, but is also referred to as pOPL2.

2. Claim Objections

G. Claim 25 is objected to. There should be a comma between the phrase "upon binding" and "internalizes." Appropriate correction is required.

H. Claims 29-34, 38, 41 are objected to since they depend from non-elected claim 1.

I. Claims 44 and 56 are objected to since commas are missing. The claims should read "...plurality of targeted agents, the targeted agents are the same..." and "...plurality of chemokine receptor targeting agents, the targeting agents are the same..."

3. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

J. Claims 29, 40, 43-45, 53, 55, 56 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is rendered indefinite because of the term "animal mammal." This rejection can be overcome by removing the term "animal."

Claim 43 is rendered indefinite because of the term "tissue damage-promoting cells. It is not clear what these cells refer to. Bacteria and fungi are tissue damage-promoting cells which cause damage during an infection.

Claims 43 and 55 are rendered indefinite since it is not clear whether the phrase "a portion thereof" refers to a targeted agent, a targeting agent, or both. Also, the phrase "a portion thereof" is part of the legal specification, but cannot be found in the formal specification. Therefore, the metes and bounds of "a portion" is not known. For example, Applicants do not disclose how they know which portion(s) of these molecules is active in treating the disease. Also it is not clear what receptor "*the* receptor" is referring to. It is suggested that the term "said receptor" be used.

Claims 44, 45 and 56 are confusing because of the phrase "plurality of. " It is not understood if the term "plurality" refers to different *types* of targeted/targeting agents, or literally two or more *molecules* of one type of agent. The phrase "where the agents are the same" makes these claims even more confusing since a plurality of the same receptors means, literally, two or more molecules.

Claims 53 and 63 are confusing. The claims make no mention of a targeted agent and recite "the chemokine receptor targeting agent and target*ing* agent" and should likely read "and target*ed* agent."

Claims 26, 28, 30-34, 37, 44-52, 56, 57 and 59-64 are rejected since they depend from rejected base claims.

4. Claim Rejections - 35 USC § 112, first paragraph – enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

K. Claims 25-38, 40 and 43-64 contain subject matter which is not described in the specification. This claim is drawn to a method of treating disorders associated with inflammatory responses associated with activation, proliferation and/or migration of immune effector cells. However, the breadth of the claims is large and Applicants provide no guidance of how to treat *every* possible disorder associated with an inflammatory response. In addition, it is not predictable to one of ordinary skill in the art how to use a method of treating a patient with *any* type of inflammatory response. Applicants do not give exact dosages or a treatment regimen, but simply state that anything needing to be determined for treating a patient can be determined by those of skill in the art. Therefore, Applicants are not enabled for this broad method.

Furthermore, it is not understood how Applicants can treat a disorder of the immune system of a patient by modulating the activation, proliferation and/or migration of inhibited immune effector cells without causing other immune-related problems to occur. While Applicants describe numerous disease states in which chemokine/toxin conjugates could *potentially* be used, Applicants give no guidance, or working examples for use of these compounds in treating patients who have these diseases. It is not predictable to one of ordinary skill in the art how to treat the disorder of interest without causing subsequent disorders due to an altered immune system. One example well known in the art is that of treating bone marrow cancer in which bone marrow cells are removed from the patient and he/she is

administered a dose of chemotherapy in which the patient is brought near death before bone marrow cells are reintroduced. For these reasons, Applicants are not enabled for this method of treatment.

Claim 40 encompasses subject matter which is not described in the specification. Bacteria and fungi, for example, are considered "tissue damage-promoting cells" since they can cause damage during an infection. Applicants are not enabled for a method of treating secondary tissue damage by inhibiting these tissue damage-promoting cells.

Claims 43 and 55 contain subject matter which is not described in the specification. This claim uses the phrase "a portion thereof." Applicants provide no guidance or working examples of how a portion of a targeting agent and/or a targeted agent can effectively bind to a cell bearing the necessary receptor and internalize, or how a portion of a targeted agent can treat a disorder associated with inflammatory responses associated with an immune effector cell. It is not predictable to one of ordinary skill in the art what portions of said agents are necessary to perform the claimed method. It has been shown that the function of a peptide cannot be determined based solely on knowing the amino acid sequence (see Rudinger et al., 1976, especially the conclusion). The possible effect of changing even one amino acid in a polypeptide can be seen in Cunningham and Wells (1989; Abstract) in which certain single substitutions of alanine in various positions of human growth hormone dramatically altered its binding affinity for the human growth hormone receptor. In addition, George et al. (1988; p. 145) states that: "Sequence-comparison methods will not be able to assess biological relatedness until the structure/function problem is more clearly understood." Claims 44-54 and 56-64 are rejected since they depend from rejected base claims.

Claims 53 and 63 contain subject matter which is not described in the specification. These claims recite linking a targeting agent with a targeting agent. The specification does not teach how linking two targeting agents can be used in the claimed method. The specification only teaches a method of treatment using a targeting agent and a target*ed* agent.

In summary, the breadth of the claims is large with regard to a method of treating disorders associated with inflammatory responses associated with activation, proliferation and/or migration of immune effector cells. In addition, Applicants provide no guidance of how to treat *every* possible disorder associated with an inflammatory response. Also, it is not predictable to one of ordinary skill in the art how to use a method of treating a patient with *any* type of inflammatory response and, furthermore, without causing subsequent disorders due to an altered immune system. Applicants provide no guidance or working examples of how a *portion* of a targeting agent and/or a targeted agent can effectively bind to a cell bearing the necessary receptor and internalize, or how a *portion* of a targeted agent can treat a disorder associated with inflammatory responses associated with an immune effector cell.

5. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

L. Claims 25-30, 33-36, 38, 40, 43-45, 47-49, 51, 52, 55-59, 61 and 62 are rejected under 35 U.S.C. 102(b) as being unpatentable by Volk et al (1994). The claims are directed to a method for treating a disorder associated with an inhibited inflammatory response associated with activation, proliferation and/or migration of immune effector cells in which the immune effector cells are leukocytes such as T- and B-lymphocytes, the inflammatory response results in secondary tissue damage and treatment is by use of a non-chemokine cytokine and a targeted agent conjugate. Volk et al. teach a method of treatment of inflammatory responses by use of a conjugate consisting of a non-chemokine cytokine (IL-2) and a targeted agent (PE40) (see p. 2498, under "Immunosupressive agents and treatment protocols") which internalizes (see p. 2502, column 2, line 15 of first full paragraph) and is associated with the activation (stimulation) of immune effector, T- and B-lymphocyte, cells (see the last line of the Abstract; also p. 2499 – second paragraph under results; and Figure 2) in which the inflammatory response results in secondary tissue damage (see "Discussion" on page 2504), or comprises secondary tissue damage (see "Immunization and measurement of immune response in vivo" on page 2498 – swelling of the footpad). Volk et al. also teach the *inhibition* of immune effector cells (see first paragraph of "Results" and Figure 1). Claims 31, 32, 37, 42, 46, 50, 53, 54, 60, 63 and 64 are objected to since they depend from rejected base claims.

6. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

M. Claim 25-38, 40 and 42-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ogata et al. in view of Volk et al..

The claims teach a method of treating disorder associated with inflammatory responses by using a chemokine receptor targeting agent linked to a targeted agent. Ogata et al. teach the production of a targeting agent (cytokine – IL4) linked to a targeted agent (toxin). This is seen in Figure 1B. Ogata et al. do not teach the use of this conjugate in treating disorders. However, Volk et al. teach do teach a method of treating an inflammatory response by use of a conjugate comprising a chemokine targeting agent and a targeted agent (IL2-PE40). Therefore, it would have been obvious to one of ordinary skill in the art to use the conjugate of Ogata et al. as taught by Volk et al. since, it is well known in the art that various cytokines are involved in the modulation of the inflammatory response by stimulating and/or inhibiting immune effector cells and that "fusion conjugates" using non-chemokine cytokines are useful to treat inflammatory disorders. For this reason, one of ordinary skill in the art would have been motivated to use the conjugate of Ogata et al. in the method of Volk et al.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
February 28, 2000

Gary L. Kunz

GARY L. KUNZ
PRIMARY EXAMINER
GROUP 1200